

April 22, 1965

Dr. Henry M. Sobell
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

Dear Henry:

You were very kind to send me a copy of your research proposal and ideas on purine-pyrimidine base pairs as you saw them from a crystallographic vantage point. On a couple of occasions I wanted to respond but preferred to wait until I could make a more meaningful comment. I think now that I had better acknowledge your thoughtfulness in sending this proposal before you think me impolite or indifferent.

From all the work that we have done with enzymatic replication and from everything that we have been told about the man's job that the boy's hydrogen bonding is reputed to be doing, we are inclined to give the polymerase a special role. This role would be the recognition of a base pair, and the subsequent diester bond formation to the chain end ~~that~~ would depend upon the proper steric conformation of the complex that comes with the recognition of the enzyme of this base pair. Whether this base pair has the Hoogsteen or the W-C configuration we of course have no ~~what~~ of knowing. We have been struck by the facility with which dAT primes the polymerase but we have attributed this to the ready breathing of the helical template. I am inclined to feel that the initiation of a de novo reaction comes from an enzymatic synthesis of oligomers; we have a dogmatic reluctance to invoke any non-enzymatic events, and this carries over to a reaction as bizarre as the in vitro development of dAT.

I hope you won't feel inhibited about speculating and working on the nature of copolymer and homopolymer syntheses and replications because of any fund of knowledge residing with those of us who have been working on this problem. It simply is too fragmentary and shallow to inhibit you from making major contributions to this area. I will be very eager to hear how things are going with you.

With best wishes,

Sincerely,

Arthur Kornberg

AK:ES